ABSTRACT OF THE DISCLOSURE

The present invention describes calcium sensitive and selective maxi-K potassium channel opener/activator compounds that function to open maxi-K channels under conditions of high intracellular calcium concentrations, and which do not significantly affect the opening of maxi-K channel proteins under conditions of low or physiologically normal intracellular calcium concentrations. Methods of assaying for and using such compounds are also provided. According to the invention, whole cell voltage patch-clamp studies newly demonstrated that the ability of opener compounds, e.g., fluoro-oxindoles and chloro-oxindoles, to open maxi-K channels was sensitive to the intracellular Ca^{2+} concentration ($[Ca^{2+}]_i$, i.e., more channels opened at more negative potentials. Particular fluoro-oxindole and chloro-oxindole compounds produced significant increases in whole-cell maxi-K potassium channel-mediated outward currents only in cells having higher $[Ca^{2+}]_i$, compared with effects in lower $[Ca^{2+}]_i$. Such compounds provide Ca^{2+}-sensitive and selective openers of maxi-K channels which show maximum effectiveness under conditions of increased $[Ca^{2+}]_i$ and, as such, provide treatments for diseases and disorders in which cells undergo, or are subject to, traumatic stress due to high internal calcium levels, such as stroke.